amended claim 1 continues to embrace nucleic acids that comprise SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:50 but which may contain sequence in addition to the afore-mentioned sequences, provided such sequences are capable of hybridizing under stringent conditions to a nucleic acid sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:50 and code for a polypeptide having RIP60 activity.

Claim 1 has been further amended to recite "nucleic acid molecule" rather than "nucleic acid molecules". This amendment does not narrow the scope of the claim.

Claim 6 has been amended to clarify the meaning of the claim. This amendment does not narrow the scope of the claim.

Claim 7 has been amended to add the term "and" prior to the last member of the Markush group. This amendment does not narrow the scope of the claim.

No new matter has been added.

Rejection of Claims Under 35 U.S.C. §112, first paragraph

Claims 1-16:

The Examiner has rejected claims 1-16 under 35 U.S.C. §112 first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) at the time the application was filed had possession of the claimed invention.

The Examiner acknowledges that SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 and SEQ ID NO:50 and nucleic acids encoding polypeptides with sequences corresponding to SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:51 meet the written description provision of 35 U.S.C. §112, first paragraph. However, the Examiner states that "the specification provides insufficient written description to support the genus (comprising) nucleic acid molecules which code for polypeptides that have RIP60 activity (including all mutants derived by deletions, additions and/or substitution): sequences that hybridize to SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 and SEQ ID NO:50 .... corresponding sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a recited degree of identity (similarity, homology), and so forth."

Applicants have amended claim 1 to remove the claim limitation "deletions, additions and substitutions of (a) which code for a polypeptide having RIP60 activity". As explained below, claim 1 as amended now satisfies the written description requirement according to the

Written Description Guidelines (the "Guidelines") published in the Federal Register on January 5, 2001.

Example 9 of the Guidelines indicates that a claim relating to an isolated nucleic acid that specifically hybridizes under highly stringent conditions to a complement of a particular sequence satisfies both the species and the genus written description requirement. The specification teaches that the disclosed sequence codes for a protein having two defined functions and sets forth hybridization conditions that are similar to those of the instant specification (6XSSC in Example 9 and 3.5XSSC in application). The Guidelines state that the disclosure of the particular species of nucleic acid is an actual reduction to practice, and is sufficient to satisfy the species written description requirement. With respect to the genus analysis, the Guidelines further state that substantial variation among species (within the genus of molecules that would hybridize) would not be expected because the hybridization limitation yields structurally similar DNAs. The Guidelines conclude that the written description requirement for the genus is met because a representative number of species is disclosed in view of the hybridization conditions, the coding function of DNA, and the skill and knowledge in the art.

As amended, claim 1 relates in part to an isolated nucleic acid molecule that hybridizes under stringent conditions to nucleic acid molecules having a sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:50 (and complements thereof). The instant specification teaches that the nucleic acid molecules hybridizing to SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:50 code for a polypeptide with RIP60 activity (as described below). In view of the Guidelines, the disclosures of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 and SEQ ID NO:50 each serve as actual reductions to practice of a species. With respect to the genus analysis, as with Example 9, substantial variation among species of molecules that hybridize to the afore-mentioned nucleic acids would not be expected given the hybridization conditions, the requisite coding function of DNA, and the skill and knowledge in the art.

The remaining claim limitation of claim 1 relates to nucleic acid molecules that differ from the genus of hybridizing molecules due to the degeneracy of the genetic code and code for polypeptides having RIP60 activity. It is within the skill and knowledge of the ordinary artisan to determine the sequence of nucleic acids degenerate to those capable of hybridizing to SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:50, using a genetic code table. (See Example 11 of the Guidelines.) Accordingly, this limitation is adequately described as well.

Example 8 of the Guidelines states that a genus claim to an isolated nucleic acid comprising a particular sequence that contains a full open reading frame (as opposed to a cDNA fragment or an EST) is adequately described by a specification that teaches the sequence of one species of nucleic acid and the function of the protein encoded by the nucleic acid. The Guidelines state that one of skill in the art can readily envision other nucleic acid sequences that include the sequence of the disclosed species, for example, vectors containing the sequence. The Guidelines conclude that when the full length open reading frame is disclosed and substantial variability within the genus arises due to addition of elements that are not part of the inventor's particular contribution, the genus of DNAs that comprise a particular sequence is adequately disclosed given the level of skill and knowledge in the art. Accordingly, claims 2 and 3 are adequately described.

Example 13 of the Guidelines indicate that a claim to an isolated protein comprising a particular amino acid sequence is adequately described because "there is relatively little variation among the species within the genus because each member of the genus shares (the sequence) as a necessary common feature." In a similar fashion, the nucleic acids of instant claims 4 and 5 which code for polypeptides comprising amino acid sequences SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:51 are also adequately described in view of Example 13 and the knowledge in the art of codons and amino acids.

In view of the foregoing amendment and arguments, Applicants respectfully request that the Examiner reconsider and withdraw his rejection of claims 1-16 under 35 U.S.C. §112 first paragraph.

Claims 1-5, 11 and 14:

The Examiner has rejected claims 1-5, 11 and 14 under 35 U.S.C. §112 first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) at the time the application was filed had possession of the claimed invention.

The Examiner states that "the specification has not provided sufficient guidance to allow one of skill in the art to practice the claimed invention without due experimentation." The Examiner further states that "in view of the lack of an enabling description to obtain, make and use the amino acid variants and fragments of the instant claims, the unpredictability associated with making and using the claimed variants and fragments of the recited sequence encompassed

in the scope of the claims as set forth above, one skilled in the art would not recognize from the disclosure that the Applicant was in possession of any of the polynucleotides encoding the variants or polypeptide fragments."

Claims 1-5 relate to nucleic acid molecules that code for polypeptides having RIP60 activity, degenerates thereof and complements of either. Claims 11 and 14 relate to expression vectors comprising such nucleic acids and host cells containing the expression vectors. As stated above, Applicants have amended claim 1 to remove reference to "deletions, additions and substitutions which code for a polypeptide having RIP60 activity." Accordingly, claim 1 as amended relates to nucleic acid molecules that hybridize to SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:50 and that code for a polypeptide having RIP60 activity (discussed below), degenerates of such nucleic acids, and complements thereof. The Examiner's assertion that "the resulting polynucleotides may or may not possess any of the biological properties of RIP60 polypeptide" is moot because the claim explicitly states that the nucleic acids must code for a polypeptide having RIP60 activity.

Applicants respectfully traverse the Examiner's assertion that "the specification fails to teach the critical protein portions that are needed to ensure the polypeptide would possess RIP60 activity." The specification teaches that RIP60 activity includes one or more of the following activities: DNA binding, protein multimerization, and nucleic acid looping (i.e., combined DNA binding and nucleic acid condensation). (See page 21, lines 24-27.) The specification further teaches that DNA binding can be attributed to the zinc finger domains of RIP60, such as for example the Z2 domain having amino acid sequence SEQ ID NO:4 and coded for by nucleic acid sequence SEQ ID NO:3. (See page 10, lines 23; page 11, lines 6-15.) Protein multimerization can be attributed to the proline rich region having amino acid sequence SEQ ID NO:6 and coded for by nucleic acid sequence SEQ ID NO:5. (See page 10, lines 11-12, 18-19, 20-21, 25-29; and page 11, lines 6.) To the extent that the Z2 domain also includes part of the proline rich region, this domain can effect protein multimerization as well. (See page 11, lines 16-20.) The Examples demonstrate the ability to isolate and test individual domains or regions or combinations thereof for their ability to bind DNA, multimerize, and loop nucleic acid. (See page 47, lines 31-37; page 48, lines 1-4.)

Applicants further traverse the Examiner's assertion that "the specification is equally silent on what effects a given modification to the disclosed polynucleotide would have on the structure and/or "biological activity" possessed by the resulting polypeptide." The specification

details mutation of several regions of the RIP60 polypeptide including the Z1 and proline rich region (see page 47, lines 31-37; page 48, lines 1-4; and Examples 3, 11, 13, and 16) and the effects of such mutations on RIP60 activity (see Examples 5-10, and 17). Assays for measuring RIP60 activity of wild-type and mutant polypeptides are described throughout the specification and particularly in Examples 1, 5-10 and 17.

Applicants respectfully request that the Examiner clarify his statements made under the written description rejection that relate to "undue experimentation" and the "unpredictability associated with making and using the claimed variants." Applicants are unclear as to whether this is intended as a written description rejection (as responded to above) or an enablement rejection.

Notwithstanding Applicants' request for clarification from the Examiner, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-5, 11 and 14 under 35 U.S.C. § 112, first paragraph for lack of written description.

Rejection of Claims Under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 1-16 under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected as being vague and indefinite by the use of the term "RIP60 activity". The Examiner states that "it is unclear which RIP60 activity Applicant is referring to." Applicants respectfully traverse this rejection because the specification defines RIP60 activity as including one or more of the following activities: DNA binding, protein multimerization, and nucleic acid looping (i.e., combined DNA binding and nucleic acid condensation). (See page 21, lines 24-27.) SEQ ID NO:1 encodes the human RIP60 polypeptide, which is capable of DNA binding, protein multimerization, and nucleic acid looping. SEQ ID NO:3 encodes the Z2 domain of human RIP60, which is capable of DNA binding, protein multimerization, and nucleic acid looping. (See page 10, lines 22-23; page 17, lines 12-13 and 18-19.) SEQ ID NO:5 encodes the proline rich region (PRR) of human RIP60, which is capable of protein multimerization. (See page 10, lines 23-25.) SEQ ID NO:50 encodes the Z2 domain and the PRR of RIP60, which together are capable of DNA binding, protein multimerization, and nucleic acid looping. Accordingly, Applicants believe that the term "RIP60 activity" is sufficiently defined in the specification to render the term definite.

Claim 1 is further rejected as being vague and indefinite by the use of the term "under stringent conditions". The Examiner states that the term is ambiguous. Applicants respectfully traverse this rejection because the specification defines stringent conditions as conditions (i.e., parameters) that allow for homologs and alleles of RIP60 nucleic acids (having at least 75%, at least 85%, at least 90%, or at least 95% nucleotide identity with RIP60 nucleic acids) to be identified using hybridization assays. (See page 22, lines 9-18.) The specification further provides an example of stringent conditions as follows:

> "hybridization at 65°C in hybridization buffer (3.5x SSC, 0.02% Ficoll, 0.02% polyvinyl pyrolidone, 0.02% Bovine Serum Albumin, 2.5mM NaH_2PO_4(pH7), 0.5% SDS, 2mM EDTA). SSC is 0.15M sodium chloride/0.15M sodium citrate, pH7; SDS is sodium dodecyl sulphate; and EDTA is ethylenediaminetetracetic acid. After hybridization, the membrane upon which the DNA is transferred is washed at 2x SSC at room temperature and then at 0.1x SSC/0.1% SDS at temperatures up to 68°C." (See page 22, lines 18-24.)

Furthermore, the specification states that there are other conditions, reagents, and so forth which can be used, and would result in a similar degree of stringency. (See page 22, lines 23-24.) The skilled artisan will be familiar with such conditions and will be able to manipulate them in order to identify homologs and alleles of RIP60 nucleic acids of the invention, which include sequences having at least 75%, at least 85%, at least 90%, or at least 95% nucleotide identity. The term stringent conditions is defined in the specification and is also known and practiced in the art on a routine basis (as evidenced for example by the Written Description Guidelines, January 5, 2001, Example 9) and accordingly, it is not indefinite.

Claim 1 is further rejected as being vague and indefinite by the use of the phrase "deletions, additions and substitutions of (a) which code for a polypeptide having RIP60 activity." The Examiner states that the phrase is confusing because "it seems that it is the polypeptides encoding the deletions, additions and substitutions of (a) have the RIP60 activity instead of the mutated polypeptide." Applicants have amended the claim to remove this phrase.

Claim 1 is further rejected as being vague and indefinite because the preamble of said claim refers to a single nucleic acid molecule while subsections (a) and (c) refer to a plurality of nucleic acid molecules. Applicants have amended the claim to make the terms consistent.

Claim 6 is rejected because it refers to sequences listed in Table 1 within the specification. The Examiner asserts that all such sequences must be recited within the claim. Applicants respectfully traverse the rejection on the basis that the claim term "sequences having

the database accession numbers of Table 1" is defined in the specification. The specification contains only one Table 1 which contains only database accession numbers. The courts have held that the specification can be referred to for the meaning of a claim term. In re Vogel, 422 F.2d 438, 441; 164 USPQ 619, 622 (CCPA 1970). Accordingly, the specification can be referred to in determining the meaning of "sequences having the database accession numbers of Table 1" and as a result, there is no confusion as to what the claim term means.

Claim 6 is further rejected because it recites the limitation "nucleotides which are not identical to." Applicants have amended the claim to rephrase the negative limitation as a positive limitation. Support for this amendment can be found in the specification on page 24, lines 15-16.

Claims 6 and 9-10 are rejected are being vague and indefinite by the use of the term "unique fragments." Applicants respectfully traverse this rejection because the specification defines unique fragments as a fragment that is a "signature" for the larger nucleic acid, and which is long enough to assure that its precise sequence is not found in molecules within the human genome outside of the RIP60 nucleic acids defined by the invention. (See page 24, lines 4-7.) The specification further states that a unique fragment exclude fragments that are completely composed of the nucleotide sequences having the database accession numbers of Table 1. (see page 24, lines 9-11.) The term "unique" is intended to take its ordinary and usual meaning. The American Heritage Dictionary defines unique as "being the only one of its kind; without an equal or equivalent; unparalleled." Accordingly, a unique (nucleic acid) fragment is a nucleic acid fragment having a sequence that is one of a kind, and which is without equal or equivalent (i.e., a sequence for which there is no equivalent in the human genome). Applicants believe that the term "unique fragment" is sufficiently defined in the specification (along with the meaning in the art) to render the term definite.

Claim 7 is rejected because it recites improper Markush language. Applicants have amended the claim to add the term "and" prior to the final member of the group, as suggested by the Examiner.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-16 under 35 U.S.C. 112, second paragraph.

Rejection of Claims Under 35 U.S.C. §102(a)

The Examiner has rejected claims 1-3 and 6-9 under 35 U.S.C. §102(a) as being anticipated by Sulston et al. (Genome Research, 8(11):1097-1108, 1998). According to the Examiner, Sulston et al. disclose the polynucleotide sequences recited SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 and SEQ ID NO:50. Applicants respectfully traverse the rejection for the reasons stated below.

The Sulston et al. reference which was published in November 1998 provides no specific sequence information, although it does refer to sequence data posted at the Sanger website. Applicants unsuccessfully attempted to search the Sanger website for sequences that were disclosed as of November 1998. If the Examiner is aware of the sequences posted on the referenced website, he is requested to forward such sequences to Applicants. In the absence of sequence information either in the reference or at the website, the Sulston et al. reference does not anticipate claims 1-3 and 6-9.

The Examiner further provides a sequence from GenBank Accession number AC005586 made by Sulston et al. which cites the Sulston et al. reference. The GenBank listing for this sequence, which is attached hereto as Appendix B, indicates that the sequence in the form cited by the Examiner was made publicly available as of September 30, 2000. (See date in upper right hand corner.)

The Examiner is reminded that the present invention claims a priority date of January 4, 1999, at which time the complete RIP60 nucleic acid sequence was disclosed by the inventors in the priority provisional applications. (See page 1, under "Related Applications".) Accordingly, for the purpose of a 102(a) prior art rejection, the sequence cited by the Examiner is not prior art because it was made publicly available (in the form cited by the Examiner) only after the priority date of the present application, and therefore cannot anticipate claims 1-3 and 6-9.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-3 and 6-9 under 35 U.S.C. §102(a) as being anticipated by Sulston et al. (Genome Research, 8(11):1097-1108, 1998).

Rejection of Claims Under 35 U.S.C. §103(a)

The Examiner has rejected claims 1-16 under 35 U.S.C. §103(a) as being unpatentable over Sulston et al. (Genome Research, 8(11):1097-1108, 1998). According to the Examiner, Sulston et al. disclose "the polynucleotide sequences recited SEQ ID NO:1, SEQ ID NO:3, SEQ

ID NO:5 and 50 (and) consequently, said reference anticipates all the limitations of the instant claims". The Examiner states that although "Sulston et al. does not explicitly disclose incorporating said polynucleotides with a promoter in an expression vector, transfecting a host cells with said vector nor using said transformed cell to express the recombinant proteins recited in the instant claims...it would be obvious to one of skill in the art to take a polynucleotide sequence, determine the open reading frames and incorporate it in a vector so the polypeptide encoded by said polynucleotide can be expressed cheaply and efficiently in a recombinant system."

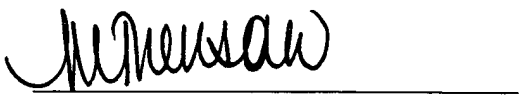
Applicants respectfully traverse the rejection for the same reasons stated above under the 102(a) rejection. Specifically, the Sulston et al. reference does not disclose the sequences presently claimed, and the GenBank sequence cited by the Examiner is not prior art under 102(a) because it was publicly available (in the form cited by the Examiner) after the priority date of the present application.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-16 under 35 U.S.C. §103(a) as being unpatentable over Sulston et al. (Genome Research, 8(11):1097-1108, 1998).

Summary

Applicants believe that each of the pending claims now is in condition for allowance. If the Examiner has any questions and believes that a telephone conference with Applicants' representative would prove helpful in expediting the prosecution of this application, the Examiner is urged to call the undersigned at (617) 720-3500.

Respectfully submitted,



Maria A. Trevisan, Reg. No. P-48,207
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, MA 02210-2211
(617)720-3500

Attorney's Docket No.: V0139/7038 (HCL/MAT)
Date: July 23, 2001
X08/10/01

APPENDIX A:

MARKED-UP CLAIMS

Please amend the claims as follows:

1. (Amended) An isolated nucleic acid molecule, comprising

(a) a nucleic acid [molecules] molecule which [hybridize] hybridizes under stringent conditions to a molecule consisting of a nucleic acid of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:50 and which [code] codes for a polypeptide having RIP60 activity,

(b) [deletions, additions and substitutions of (a) which code for a polypeptide having RIP60 activity,

(c)] a nucleic acid [molecules] molecule that [differ] differs from the nucleic acid [molecules] molecule of (a) [or (b)] in codon sequence due to the degeneracy of the genetic code, and

[(d)] (c) complements of (a)[,] or (b) [or (c)].

2. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule comprises SEQ ID NO:1.

3. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule comprises SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:50.

4. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule codes for a polypeptide comprising SEQ ID NO:2.

5. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule codes for a polypeptide comprising SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:51.

6. (Amended) An isolated nucleic acid molecule selected from the group consisting of

(a) a unique fragment of nucleic acid molecule of SEQ ID NO:1, and

(b) complements of (a),

provided that the unique fragment includes a sequence of contiguous nucleotides [which is not identical to] other than the exact sequence of any sequence selected from the sequence group consisting of

(1) sequences having the database accession numbers of Table 1,

(2) complements of (1), and

(3) fragments of (1) and (2).

7. (Amended) The isolated nucleic acid molecule of claim 6, wherein the sequence of contiguous nucleotides is selected from the group consisting of:

(1) at least two contiguous nucleotides nonidentical to the sequence group,

(2) at least three contiguous nucleotides nonidentical to the sequence group,

(3) at least four contiguous nucleotides nonidentical to the sequence group,

(4) at least five contiguous nucleotides nonidentical to the sequence group,

(5) at least six contiguous nucleotides nonidentical to the sequence group, and

(6) at least seven contiguous nucleotides nonidentical to the sequence group.

8. The isolated nucleic acid molecule of claim 6 or 7, wherein the fragment has a size selected from the group consisting of at least: 8 nucleotides, 10 nucleotides, 12 nucleotides, 14 nucleotides, 16 nucleotides, 18 nucleotides, 20, nucleotides, 22 nucleotides, 24 nucleotides, 26 nucleotides, 28 nucleotides, 30 nucleotides, 50 nucleotides, 75 nucleotides, 100 nucleotides, and 200 nucleotides.

9. The isolated nucleic acid molecule of claim 6 or 7, wherein the unique fragment encodes a peptide which is a fragment of a polypeptide consisting of SEQ ID NO:2.

10. The isolated nucleic acid molecule of claim 8, wherein the unique fragment encodes a peptide which is a fragment of a polypeptide consisting of SEQ ID NO:2.

11. An expression vector comprising the isolated nucleic acid molecule of claims 1, 2, 3, 4 or 5 operably linked to a promoter.

12. An expression vector comprising the isolated nucleic acid molecule of claim 9, operably linked to a promoter.

13. An expression vector comprising the isolated nucleic acid molecule of claim 10, operably linked to a promoter.

14. A host cell transformed or transfected with the expression vector of claim 11.

15. A host cell transformed or transfected with the expression vector of claim 12.

16. A host cell transformed or transfected with the expression vector of claim 13.